

CLAIMS

We claim:

1. A method of screening drug candidates comprising:
 - a) providing a cell that expresses recombinant human KSP or a fragment thereof;
 - b) adding a drug candidate to said cell under conditions where the drug candidate is taken up by the cell; and
 - c) determining the effect of said drug candidate on the bioactivity of said recombinant human KSP.
2. The method of claim 1 wherein said effect is determined by determining the effect on cellular proliferation.
3. The method of claim 1 wherein said effect is determined by determining the effect on cellular viability.
4. The method of claim 1 wherein said effect is determined by determining the effect on cellular morphology.
- 15 5. The method of claim 1 wherein said effect is determined by determining the effect on the mitotic spindle.
6. The method of claim 1 wherein said effect is determined by determining the effect on the ATP hydrolysis.
7. The method of claim 1 wherein said effect is determined by determining the effect on apoptosis.
- 20 8. The method of claim 1 wherein said effect is determined by determining the effect on necrosis.
9. The method of claim 1 wherein said cell is a cancer cell.
10. The method of claim 9 wherein said effect is determined by determining the effect on cancer growth.
- 25 11. The method of claim 1 wherein said cell is an endothelial cell.

12. The method of claim 11 wherein said effect is determined by determining the effect on angiogenesis.

13. The method of claim 1 wherein said cell is a metastatic cancer cell.

14. A method of screening for a bioactive agent capable of binding to a cellular proliferation protein, wherein said cellular proliferation protein is human KSP or a fragment thereof, said method comprising combining said cellular proliferation protein and a candidate bioactive agent, wherein said candidate bioactive agent is an exogenous agent, and determining the binding of said candidate agent to said cellular proliferation protein.

15. A method of screening for a candidate protein capable of binding to a cellular proliferation protein, wherein said cellular proliferation protein is KSP or a fragment thereof, said method comprising combining a nucleic acid encoding said cellular proliferation protein and a nucleic acid encoding a candidate protein, wherein an identifiable marker is expressed wherein said candidate protein binds to said cellular proliferation protein.

16. A method for screening for a bioactive agent capable of interfering with the binding of a cellular proliferation protein, wherein said cellular proliferation protein is KSP or a fragment thereof, and an antibody which binds to said cellular proliferation protein, said method comprising:
a) combining a cellular proliferation protein, wherein said cellular proliferation protein is KSP or fragment thereof, a candidate bioactive agent and an antibody which binds to said cellular proliferation protein; and
b) determining the binding of said cellular proliferation protein and said antibody.

17. A method for screening for a bioactive agent capable of modulating the activity of a cellular proliferation protein, wherein said cellular proliferation protein is human KSP or a fragment thereof, said method comprising combining said cellular proliferation protein and a candidate bioactive agent, wherein said candidate bioactive agent is an exogenous agent, and determining the effect of said candidate agent on the activity of said cellular proliferation protein.

18. A method of screening drug candidates comprising:
a) providing a cell that expresses KSP;
b) adding a drug candidate to said cell; and
c) determining the effect of said drug candidate on the expression of KSP.

19. The method of claim 18 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate, wherein the concentration of said drug candidate can vary when present, and wherein said comparison can occur after addition or removal of the drug candidate.

5 20. The method of claim 18 wherein the expression of said KSP is decreased as a result of the introduction of the drug candidate.

21. The method of claim 18 wherein said cell is a tumor cell.

22. A method of evaluating the effect of a candidate cellular proliferation drug comprising:

- a) administering said drug to a patient;
- b) removing a cell sample from said patient; and
- c) determining the expression profile of said cell, wherein said expression profile includes a KSP gene.

10 23. A method of claim 22 further comprising comparing said expression profile to an expression profile of a healthy individual.

15 24. The method of claim 22 wherein said sample is a blood sample.

25. The method of claim 22 wherein said sample is a urine sample.

26. The method of claim 22 wherein said sample is a buccal sample.

27. The method of claim 22 wherein said sample is from a PAP smear.

28. The method of claim 22 wherein said sample is from cerebral spinal fluid.

20 29. The method of claim 22 wherein said sample is from breast tissue.

30. The method of claim 22 wherein said sample is from lung tissue.

31. The method of claim 22 wherein said sample is from colon tissue.

32. The method of claim 22 wherein said patient has cancer.

33. A method of evaluating the effect of a candidate cellular proliferation drug comprising:
a) administering said drug to a patient wherein said patient has cancer and has been identified
as expressing KSP at a level higher than an individual not having cancer;
b) removing a cell sample from said patient; and
c) determining the effect on KSP activity, wherein said KSP activity is mitosis.

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34. A method of diagnosing a hyper-proliferative disorder in an individual comprising determining
the level of expression a KSP gene in an individual and comparing said level to a standard or control
level of expression, wherein an increase indicates that the individual has a hyper-proliferative disorder.

35. The method of claim 34 wherein said disorder is cancer.

10 36. A method for inhibiting cellular proliferation, said method comprising administering to a cell a
composition comprising an antibody to KSP, wherein said antibody is conjugated to a ligand.

37. The method of claim 36 wherein said ligand is tumor cell specific.

38. The method of claim 36 wherein said ligand facilitates said antibody entry to said cell.

39. The method of claim 36 wherein said cell is a cell of an individual.

15 40. The method of claim 39 wherein said individual has cancer.

41. The method of claim 36 wherein said antibody is a humanized antibody.

42. A method for inhibiting cellular proliferation in a cell, wherein said method comprises
administering to a cell a composition comprising antisense molecules to KSP.

20 43. A method for inhibiting cellular proliferation, said method comprising administering to a cell a
composition comprising an inhibitor of KSP.

44. The method of claim 43 wherein said KSP is human KSP.

45. The method of claim 43 wherein said KSP is a fragment of human KSP.

46. The method of claim 43 wherein said inhibitor is a small molecule.

47. The method of claim 43 wherein said small molecule has a molecular weight of between 50 kD and 2000 kD.

48. The method of claim 46 wherein said composition further comprises an acceptable pharmaceutical carrier.

49. The method of claim 48 wherein said composition is for parenteral administration.

50. The method of claim 48 wherein said composition is for oral administration.

51. The method of claim 48 wherein said composition is for topical administration.

52. The method of claim 43 wherein said cell is in an individual.

10 53. The method of claim 52 wherein said individual has cancer.

54. The method of claim 52 wherein said individual is at risk for restenosis.

55. The method of claim 43 wherein said cell is an endothelial cell.

56. The method of claim 43 wherein said cell is a metastatic cancer cell.

57. The method of claim 53 wherein said inhibiting is by disruption of mitosis.

15 58. The method of claim 53 wherein said inhibiting is by induction of apoptosis.

59. A biochip comprising a nucleic acid segment from KSP, wherein said biochip comprises fewer than 1000 nucleic acid probes.